There further exists a need for a positively charged membrane that has low non-specific binding for biomolecules. There further exists a need for a positively charged membrane that involves a relatively simple chemistry, and at the same time permits the degree of crosslinking to be controlled with ease.

These advantages of the present invention, as well as additional inventive features, will be apparent from the description of the invention provided herein.

U.S. Patent 4,473,474 discloses a cationic charge modified microporous membrane. The membrane comprises a hydrophilic organic polymeric microporous membrane and a charge modified amount of primary cationic modifying agent bonded to the wetted surfaces of the membrane. The primary charge modifying agent is a water soluble organic polymer having a molecular weight greater than about 1000 wherein each monomer thereof has at least one epoxy group capable of bonding to the surface of the membrane and at least one tertiary amine or quaternary ammonium group. U.S. Patent 4,601,828 discloses a method of transferring macromolecules such as nucleic acid and proteins from a chromatographic substrate to an immobilizing matrix. The immobilizing matrix is a charged modified microporous membrane comprising an organic microporous membrane having a charge modifying amount of a cationic charge modifying agent bonded to the wetted surfaces of the membrane.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 depicts the breakthrough curve for bovine serum albumin (BSA) obtained on a membrane according to an embodiment of the present invention. The x-axis represents the filtration time, and the y-axis represents the absorbance of the filtrate at 280 nm and is indicative of the concentration of BSA. See Example 1 for additional details.

Fig. 2 depicts the breakthrough curve for BSA obtained on a membrane according to another embodiment of the present invention. The x-axis and the y-axis are as described in Fig. 1. See Example 5 for additional details.

Fig. 3 depicts the breakthrough curve for bovine serum albumin (BSA) obtained on a membrane according to yet another embodiment of the present invention. The x-axis and the y-

axis are as described in Fig. 1. See Example 8 for additional details.

BRIEF SUMMARY OF THE INVENTION

Many of the foregoing needs have been fulfilled by the present invention which provides a positively charged microporous membrane comprising a porous substrate and a crosslinked coating having pendant cationic groups. In some embodiments, the crosslinked coating comprises a crosslinked polyamine such as a polyalkyleneamine. In a preferred

WHAT IS CLAIMED IS:

1. A positively charged microporous membrane comprising a porous substrate and a crosslinked coating having pendant positively charged groups.

2. The positively charged microporous membrane of claim 1, wherein the porous substrate is hydrophilic.

3. The positively charged microporous membrane of claim 1 or 2, wherein the crosslinked coating comprises a crosslinked polyamine.

4. The positively charged microporous membrane of claim 3, wherein the polyamine includes a polyalkyleneamine.

5. The positively charged microporous membrane of any of claims 1-4, wherein the crosslinked coating includes a diallylamine copolymer.

6. The positively charged microporous membrane of any of claims 1-4, wherein the crosslinked coating includes an acrylic copolymer.

7. The positively charged microporous membrane of claim 1 or 2, wherein the crosslinked coating is prepared by crosslinking a composition comprising a diallylamine copolymer having epoxy groups and pendant positively charged groups, a polyalkyleneamine, and an amine reactive compound having a positively charged group.

8. The positively charged microporous membrane of claim 1 or 2, wherein the crosslinked coating includes a copolymer of diallylamine, diallyldialkylammonium halide, acrylic monomer having a quaternary ammonium group, and a crosslinking agent.

9. The positively charged microporous membrane of claim 1 or 2, wherein the crosslinked coating includes an acrylic polymer having epoxy groups and pendant positively charged groups and

a copolymer comprising a polyamine and a glycidyl compound having a positively charged group.

10. The positively charged microporous membrane of claim 4, wherein the polyalkyleneamine is polyethyleneimine.

B4 11. The positively charged microporous membrane of any of claims 1-10, wherein the positively charged group includes quaternary ammonium groups.

12. The positively charged microporous membrane of any of claims 1-10, wherein the positively charged group is linked through a spacer group.

13. The positively charged microporous membrane of claim 12, wherein the spacer group includes one or more moieties selected from the group consisting of hydroxy, hydroxyalkyl, amino, aminoalkyl, amido, alkylamido, ester, and alkoxyalkyl.

14. The positively charged microporous membrane of claim 12, wherein the spacer group includes one or more moieties selected from the group consisting of hydroxyalkyl, alkylamino, hydroxyalkylaminoalkyl, hydroxyalkylaminoalkyl hydroxyalkyl, alkylaminoalkyl, and alkylamido.

B5 15. The positively charged microporous membrane of claim 5 or 6, wherein the diallylamine copolymer or acrylic copolymer includes a polymerized acrylic monomer.

16. The positively charged microporous membrane of claim 15, wherein the acrylic monomer is an acryloylaminoalkyl or acryloyloxyalkyl monomer.

17. The positively charged microporous membrane of claim 5, wherein the diallylamine copolymer includes one or more polymerized nitrogen containing comonomers.

18. The positively charged microporous membrane of claim 17, wherein the one or more polymerized nitrogen containing

comonomers are selected from the group consisting of comonomers carrying quaternary ammonium groups and comonomers carrying tertiary amino groups.

19. The positively charged microporous membrane of claim 8, wherein the crosslinking agent is an N-(alkoxymethyl)acrylamide.

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20. The positively charged microporous membrane of claim 8 or 19, wherein the acrylic monomer is an acryloylaminoalkyl or acryloyloxyalkyl trialkylammonium halide.

21. The positively charged microporous membrane of claim 6, wherein the acrylic copolymer comprises a polymerized monomer selected from the group consisting of glycidylalkylacrylate, methacryloyloxyalkyl trialkylammonium halide, and methacryloylaminoalkyl trialkylammonium halide.

22. The positively charged microporous membrane of claim 6, wherein the acrylic copolymer is linked to a polyamine.

23. The positively charged microporous membrane of claim 22, wherein the polyamine is pentaethylenehexamine.

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24. The positively charged microporous membrane of claim 11, wherein the positively charged group is linked to the polyethyleneimine through a reaction with a glycidyl compound having a positively charged group.

25. The positively charged microporous membrane of claim 11 or 24, wherein the coating is crosslinked through a reaction with a polyglycidyl compound.

26. The positively charged microporous membrane of any of claims 1-25, wherein the porous substrate comprises a substrate polymer.

27. The positively charged microporous membrane of claim 26, wherein the substrate polymer is selected from the group

consisting of polyaromatics, polysulfones, polyolefins, polystyrenes, polyamides, polyimides, fluoropolymers, polycarbonates, polyesters, cellulose acetates, and cellulose nitrates.

28. The positively charged microporous membrane of claim 27, wherein the substrate polymer is a polysulfone.

29. A positively charged microporous membrane having a protein binding capacity of about 25 mg/ml or greater comprising a porous substrate and a crosslinked coating that includes a pendant positively charged group.

30. The positively charged microporous membrane of claim 29, wherein the protein is bovine serum albumin or immunoglobulin.

B8 31. The positively charged microporous membrane of claim 29 or 30, wherein the porous substrate is hydrophilic.

32. A process for preparing a positively charged microporous membrane comprising a porous support and a diallylamine copolymer having pendant positively charged groups linked to the diallylamine copolymer through spacer groups, the process comprising:

(a) providing a porous substrate;

(b) contacting the porous substrate with a composition comprising a diallylamine copolymer having epoxy and pendant positively charged groups, a polyalkyleneamine, and an amine reactive compound having a positively charged group;

(c) curing the substrate obtained in (b) to obtain the positively charged membrane; and

(d) optionally, extracting the membrane obtained in (c) to remove extractable residue therein.

33. The process of claim 32, wherein the polyalkyleneamine comprises pentaethylenehexamine.

B9 34. The process of claim of claim 32 or 33, wherein the amine reactive compound is a glycidyl trialkylammonium halide.

35. The process of claim 32, wherein the diallylamine copolymer includes an acrylic monomer.

36. The process of claim 35, wherein the diallylamine copolymer is prepared by a process comprising (a) polymerizing a mixture of diallylamine and methacryloylaminopropyl trimethylammonium chloride to obtain a polymer and (b) contacting the polymer obtained in (a) with epichlorohydrin.

37. The process of claim 36, wherein the diallylamine copolymer includes one or more nitrogen containing comonomers.

38. The process of claim 37, wherein the nitrogen containing comonomers are selected from the group consisting of comonomers carrying quaternary ammonium groups and comonomers carrying tertiary amino groups.

39. The process of claim 37, wherein the nitrogen containing comonomers are selected from the group consisting of diallyldimethylammonium chloride, dimethylaminopropyl methacrylamide, methacryloylaminopropyl trimethylammonium chloride, and combinations thereof.

B10 40. The process of claim 33, wherein the polyalkyleneamine comprises pentaethylenehexamine.

41. The process of claim 40, wherein the coating composition includes a crosslinking agent.

42. The process of claim 41, wherein the crosslinking agent is a polyglycidyl compound.

B11 43. A process for preparing a microporous membrane comprising a porous support and a diallylamine copolymer having pendant positively charged groups linked to the diallylamine copolymer through spacer groups, the process comprising:

(a) providing a porous substrate;

(b) contacting the substrate with a composition comprising a copolymer of a diallylamine, diallyldialkylammonium halide, an acrylic monomer having a quaternary ammonium group, and a crosslinking agent;

(c) curing the substrate obtained in (b) to obtain the positively charged membrane; and

(d) optionally, extracting the membrane obtained in (c) to remove extractable residue therein.

44. The process of claim 43, wherein the crosslinking agent is an N-(isobutoxymethyl)-acrylamide.

45. The process of claim 43 or 44, wherein the acrylic monomer having a quaternary ammonium group is an acrylamide or acrylic ester having a quaternary ammonium group.

46. A process for preparing a microporous membrane comprising a porous support and an acrylic polymer having pendant positively groups linked to the acrylic polymer:

(a) providing a porous substrate;

(b) contacting the substrate with a composition comprising an acrylic copolymer having pendant positively charged groups and epoxy groups and a polyalkyleneamine modified to have pendant positively charged groups;

(c) curing the substrate obtained in (b) to obtain the positively charged membrane; and

(d) optionally, extracting the membrane obtained in (c) to remove extractable residue therein.

47. The process of claim 46, wherein the acrylic copolymer comprises a glycidylalkylacrylate and a methacryloyloxyalkyl or methacryloylaminoalkyl trialkylammonium halide.

48. The process of claim 46, wherein the polyalkyleneamine comprises a pentaethylenehexamine.

49. The process of claim 48, wherein the pentaethylenehexamine is a pentaethylenehexamine which has been modified by glycidyl trimethylammonium chloride.

50. A process for preparing a positively charged microporous membran comprising a porous substrate and a crosslinked coating comprising a polyalkyleneamine having pendant positively charged groups, the process comprising:

(a) providing a porous substrate;

(b) contacting the substrate with a coating composition comprising a crosslinking agent and the polyalkyleneamine;

(c) curing the substrate obtained in (b) to obtain a positively charged membrane; and

(d) optionally, extracting the membrane obtained in (c) to remove extractable residue therein.

B3 51. The process of any of claims 32, 43, 46, and 50, wherein the positively charged group is quaternary ammonium.

52. The process of claim 50, wherein the polyalkyleneamine comprises polyethyleneimine.

53. The process of claim 50, wherein the positively charged group is linked to the polyalkyleneamine through a spacer group.

54. The process of claim 53, wherein the spacer group includes one or more moieties selected from the group consisting of hydroxy, hydroxyalkyl, amino, aminoalkyl, amido, alkylamido, ester, and alkoxyalkyl.

55. The process of claim 53, wherein the spacer group includes one or more moieties selected from the group consisting of hydroxyalkyl, alkylamino, hydroxyalkylaminoalkyl, hydroxyalkylaminoalkyl hydroxyalkyl, alkylaminoalkyl, and alkylamido.

56. The process of claim 52, wherein the cationic group is linked to the polyethyleneimine by reaction with a glycidyl compound having a positively charged group.

57. The process of claim 56, wherein the glycidyl compound is glycidyl trimethylammonium chloride.

B14 58. The process of any of claims 50 and 52-57, wherein the coating is crosslinked by a polyglycidyl compound.

59. The process of claim 58, wherein the polyglycidyl compound is a polyalkyleneglycol polyglycidylether.

B15 60. The process of any of claims 32-59, wherein the extraction is carried out in water.

61. The process of any of claims 32-59, wherein the porous substrate is hydrophilic.

62. The process of any of claims 32-61, wherein the porous substrate comprises a polymer.

63. The process of claim 62, wherein the porous substrate comprises a polymer selected from the group consisting of polyaromatics, polysulfones, polyolefins, polystyrenes, polyamides, polyimides, polycarbonates, polyesters, fluoropolymers, and cellulosic polymers.

B16 64. The process of claim 62, wherein the porous substrate comprises polysulfone.

65. The membrane prepared by the process of any of claims 32-64.

66. A device comprising the positively charged microporous membrane of any of claims 1-55 and 65.

67. A process for separating negatively charged material from a fluid, the process comprising placing the fluid in contact with the positively charged microporous membrane of any of claims 1-32 and 65 so as to adsorb or absorb the negatively charged material to the membrane.

68. The process of claim 67, wherein the negatively charged materials include biomolecules.

69. The process of claim 68, wherein the biomolecule is selected from the group consisting of polypeptides, amino acids, nucleic acids, and combinations thereof.

B17 70. The process of claim 67, wherein the negatively charged materials include nucleic acids, endotoxins, host cell proteins, viruses, and lipids.

71. The process of claim 67, wherein a nucleic acid is separated from a fluid comprising nucleic acid and protein.

B18 72. The process of claim 70, wherein the protein is an antibody.

73. The process of claim 70, wherein the virus is an adenovirus.

74. A positively charged microporous membrane having a nucleic acid binding capacity of about 5 mg/ml or more comprising a porous substrate and a crosslinked coating that includes a pendant positively charged group.

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AMENDED SHEET